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Epidemiological Bases for the Current Ambient Carbon Monoxide Standards

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Carbon monoxide is widely distributed in the environment, and acute or chronic toxic effects may be of considerable public health significance. A review of the basis for current ambient standards is given. Mortality and morbidity studies have been negative or equivocal in relating carbon monoxide levels to health effects, but studies in human subjects with compromised coronary or peripheral circulation support an effect of acute exposure to CO at blood levels equivalent to about 20 ppm over several hours. It is possible that some of the cardiovascular effects of smoking may be related to the high levels of CO in cigarette smoke, but it has been difficult to isolate the contribution of CO independent of the effects of other smoke constituents.

Introduction

The relationship between carbon monoxide exposure and health has been extensively reviewed. The Committee on Medical and Biological Effects of Environmental Pollution of the National Academy of Sciences issued a report in 1977 (*1*). A workshop on carbon monoxide and cardiovascular disease was held in Berlin, Germany, October 1978 and the proceedings subsequently published (*2*). This report will be primarily concerned with the evidence related to the ambient carbon monoxide standard with particular emphasis on the information available since 1978.

The current ambient carbon monoxide standard is an 8-hr annual average, maximum of 9 ppm and a maximum 1-hr level of 35 ppm not to be exceeded more than once a year (Table 1) (*3*). The occupational standard is higher and is aimed at keeping the carboxyhemoglobin levels in the blood below 5% (*4*).

The ambient standard was based on the effects of elevated carboxyhemoglobin levels on the cardiovascular system and behavioral responses, especially vigilance tasks, in which the individual was asked to report the occurrence of occasional signals over long periods (*1*). The physiological bases of carbon monoxide cardiovascular effects and behavioral changes have been extensively reviewed (*1*).

Table 1. Air quality standards for carbon monoxide.[a]

		CO, ppm
Primary	1 hr annual maximum[b]	35
Secondary	8 hr annual maximum	9

[a]U.S. EPA standard (*3*).
[b]Not to be exceeded more than once per year.

The physical properties of carbon monoxide and the methods of conversion between various environmental measures of carbon monoxide are shown in Table 2. Ambient carbon monoxide levels are sometimes reported as parts per million (ppm) and/or as milligrams per cubic meter (mg/m^3) (*5*).

The occupational standard proscribes exposure by any worker to a concentration greater than 35 ppm determined as a time-weighted average exposure for an 8-hr work day. No level of carbon monoxide to which workers are exposed can exceed a ceiling concentration of 200 ppm. Workers with overt cardiovascular disease may not be protected at 35 ppm and should be included in a medical program of preplacement and periodic examinations. Such a medical program could also provide the opportunity for conducting antismok-

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ing programs for high-risk employees. WHO and NIOSH recommend that the maximal allowable carboxyhemoglobin blood level not exceed 5%.

The relationship between environmental carbon monoxide exposure and blood carboxyhemoglobin levels is primarily related to the concentration of carbon monoxide in expired air, the duration of exposure and respiratory ventilation (Table 3). The alveolar carbon monoxide levels can be crudely converted to carboxyhemoglobin by dividing the carbon monoxide in ambient air in ppm by 7. The half-life of carboxyhemoglobin in the blood is about 4 hr.

The major source of carbon monoxide is cigarette smoking. The other key sources are transportation, industry and home heating. The relationship between cigarette smoking and expired air carbon monoxide levels and carboxyhemoglobin levels in the blood are well known. Expired air carbon monoxide or carboxyhemoglobin is often used as an indicator for cigarette smoking dose. Cigarette smoking exposes the pulmonary capillary bed to about 400 ppm of carbon monoxide. Whether carbon monoxide, nicotine or tar are the key factors in the relationship between cigarette smoking and increased risk of heart attack has not been firmly established. However, important clinical, experimental evidence, especially by Aronow et al. (2), as well as many physiological studies of carbon monoxide exposure and myocardial metabolism and blood flow, certainly suggests that carbon monoxide plays an important, if not the primary, role in the relationship between cigarette smoking and cardiovascular disease. Furthermore, most evidence now suggests that the predominant effect of cigarette smoking is probably related to the acute onset of a heart attack rather than to the development of underlying atherosclerosis. Cigarette smokers living in countries in which the diet is low in cholesterol and saturated fat do not generally have extensive coronary atherosclerosis nor a very high risk of heart attack (*6*). Individuals who quit smoking have a fairly rapid drop in their risk of a heart attack (*7*). Both of these factors would suggest that the effects of carbon monoxide or cigarette smoking are probably on the acute precipitation of a heart attack.

The importance of passive smoking, that is, exposure to cigarette smoke produced by another individual, in raising the carboxyhemoglobin levels and increasing the risk of disease is a controversial subject. Recent studies suggest that passive smoking could be an important source of population exposure to carbon monoxide for nonsmokers and to disease especially in poorly ventilated areas (*8*). The recently reported startling increase in lung cancer among nonsmoking wives of Japanese men who smoke cigarettes could have important implications if verified by further studies (*9*).

There are numerous occupational sources of carbon monoxide. Michael (2) et al. recently compiled a long list of job titles associated with possible carbon monoxide exposures. There is solid evidence that workers in certain occupations are exposed to high carbon monoxide levels and elevations of carboxyhemoglobin levels, especially if they are also cigarette smokers (*10*). A study of blast furnace workers, for example, has shown that these men have carboxyhemoglobin levels two to three times as high as among nonexposed controls, and they also have a substantial increase in their carboxyhemoglobin levels in the blood from the beginning to the end of their work shift (Table 4).

Nationwide estimates of carbon monoxide emissions demonstrate a continuing downward trend (Table 5) (*1*). This is primarily related to a

Table 2. Physical properties of carbon monoxide.[a]

Property	Value
Molecular weight	28.01
Melting point	−207°C
Boiling point	−192°C
Specific gravity relative to air	0.968
Density	
At 0°C, 760 mm Hg	1.25 g/L
At 25°C, 760 mm Hg	1.15 g/L
Explosive limits in air	12.5 to 74.2% (volume)
Solubility[b]	
At 0°C	3.54 mL/100 mL water
At 25°C	2.14 mL/100 mL water
Conversion factors	
At 0°C, 760 mm Hg	1 mg/m^3 = 0.800 ppm
	1 ppm = 1.250 mg/m^3
At 25°C, 760 mm Hg	1 mg/m^3 = 0.874 ppm
	1 ppm = 1.145 mg/m^3

[a]Data from US PHEW (*5*).
[b]Volume of CO indicated is at 0°C, 760 mm Hg.

Table 3. Relationship between carboxyhemoglobin and alveolar carbon monoxide.
COHB% = 0.14 alveolar CO ppm + 0.26

Factor
Concentration of carbon monoxide in breathing atmosphere
Exposure duration
Respiratory ventilation
Blood volume
Barometric pressure
Diffusibility of the lungs from CO
Rate of CO production (endogenous)
Exact ratio of the affinity of blood for CO or O_2

Table 4. Carboxyhemoglobin levels at the beginning and end of a single shift related to smoking habits in blast furnace and control groups (1962).[a]

Use of tobacco	Group	No. in group	COHb, % saturation			
			Beginning of shift		End of shift	
			Mean	Range	Mean	Range
Nonsmokers	Blast furnace	11	2.4	1.3-4.9	4.9	2.3-14.9
	Control	21	1.3	0.8-2.1	1.5	0.9- 2.4
Usually <20 cigarettes/day	Blast furnace	26	4.5	1.3-7.3	6.2	2.5-11.9
	Control	24	3.1	0.9-6.6	3.2	1.1- 6.3
Usually >20 cigarettes/day	Blast furnace	20	5.6	3.7-7.5	7.4	4.4-11.8
	Control	18	3.7	2.0-5.5	4.0	2.2- 6.1

[a]Data of Jones and Sinclair (*10*).

Table 5. Nationwide estimates of carbon monoxide emissions: 1940-75.[a]

Source category	Emissions, 10^6 metric tons/yr (10^9 kg/yr)[b]							
	1940	*1950*	*1960*	*1968*	*1969*	*1970*	*1972*	*1975*[c]
Transportation	31.7	50.2	75.7	102.5	101.6	100.6	70.4	66.5
Industrial process losses	31.1	17.1	16.1	7.7	10.9	10.3	15.8	13.3
Agricultural burning	8.3	9.4	11.2	12.6	12.5	12.5	1.5	0.8
Fuel combustion in stationary sources	5.6	5.1	2.4	1.8	1.6	0.7	1.1	1.3
Solid-waste disposal	1.6	2.4	4.6	7.3	7.2	6.6	4.5	3.4
Miscellaneous	17.2	9.1	5.8	4.9	5.7	4.1	4.2	1.7
Total	77.5	93.3	115.8	136.8	139.5	134.8	97.5	87.0

[a]NAS data.
[b]To convert to U.S. short tons, multiply by 1.1 (1 short ton = 2×10^3lb).
[c]Annual emission as of March 12, 1975.

decrease in automobile exhaust emissions of carbon monoxide. The decrease in emissions is also reflected in a decline in ambient carbon monoxide levels in the community.

The importance of transport sources of carbon monoxide has been previously evaluated by studying the changes in carboxyhemoglobin and expired air carbon monoxide among individuals exposed to freeway traffic or heavy city congestion. The Environmental Protection Agency estimates that 42% of the U.S. population living on 2% of the U.S. land is reasonably heavily exposed to carbon monoxide (>300 tons/mi^2/yr).

A much better way of determining carbon monoxide exposure is by measuring blood carboxyhemoglobin levels. Several previous studies have attempted to measure the distribution of carboxyhemoglobin levels among selected population samples, such as blood donors or industrial workers. These studies have also been limited by the relatively crude method of estimating low levels of carboxyhemoglobin.

Radford et al. (*11*) recently studied carboxyhemoglobin levels among participants in the Health and Nutrition Survey II (Hanes II Study). Both children and adults were included in the study. Sensitive techniques were utilized for measuring carboxyhemoglobin levels and the sample is a reasonable estimate of the U.S. population. Information about cigarette smoking, residence and season of the year were also collected. The levels were measured for both children and adults. The adult population was divided into those who smoked and those who did not smoke. The levels in the children and nonsmoking adults were reasonably comparable (Table 6) (*11*). The higher levels of carboxyhemoglobin in the winter as compared to the spring or summer among nonsmokers could reflect home heating sources (indoor air pollution).

Table 6. Percent carboxyhemoglobin by season for nonsmokers (cigarette).[a]

Season	Age	Carboxyhemoglobin, %
Nov.-March	2-11	0.85
	12-74	1.03
May-Sept.	2-11	0.58
	12-74	0.70

[a]Data of Radford et al. (*11*).

The carboxyhemoglobin levels were substantially higher for cigarette smokers than nonsmok-

ers. Approximately 80% of cigarette smokers had carboxyhemoglobin levels that were greater than 2%. Note, however, that 6.4% of the nonsmoking population had carboxyhemoglobin levels greater than 2% the goal of the ambient standard. Therefore in the U.S. population there may be over 10,000,000 nonsmokers who have carboxyhemoglobin levels above the goal of the ambient standards.

The carboxyhemoglobin levels were also correlated with the degree of urbanization among noncigarette smokers. However, the effects of urbanization were relatively small as compared to that due to cigarette smoking (*11*). The levels reported by Radford are lower than those previously noted (*12*). Differences in the methods of measurement of carboxyhemoglobin, better delineation of smokers from nonsmokers and differences in the population sample may be factors which account for these differences or possibly improvement in air quality.

The health effects of carbon monoxide are determined by several factors besides the carboxyhemoglobin levels (*13*). The major determinants, however, are the carboxyhemoglobin levels in the blood, duration of exposure, work effect and health status. The last point is very critical since high risk individuals are likely to be exposed to pollution that may be detrimental to their health but be inconsequential for the vast majority of the population.

Four types of studies have been done that relate levels of carbon monoxide to health, especially to cardiovascular disease: community studies, clinical experimental, occupational and animal laboratory experimental studies.

The community studies are of the classical type. The levels of pollution, in this case ambient carbon monoxide levels, are correlated with hospital admissions, deaths or symptomatology. Usually no attempt has been made to relate the "dose" of the pollutant to any specific individual or to their disease. These "ecological" models have been discussed in great detail (*1*). Earlier studies have been done in Los Angeles (*14*) and Baltimore (*15*).

A more recent report from Denver included emergency room visits for cardiovascular complaints and ambient carbon monoxide levels (*16*). Denver has high carbon monoxide levels, similar to those in Los Angeles, and, because of the altitude of the city and the lower partial pressure of oxygen in the air, individuals are more likely to have health effects related to these levels. The visits to the emergency room related to carbon monoxide levels both as a proportion of total emergency room visits and as a daily frequency of cardiovascular complaints. The correlations are relatively weak but significant because of the large number of days included in the anaylsis. The one hour maximum ambient carbon monoxide levels for the high carbon monoxide days was 27.3 as compared to 12.1 for the low days. Other pollutants apparently did not correlate with the carbon monoxide levels in the air. The interaction of weather changes, and possibly infections were not included in the analysis.

Unlike other pollutants, the individual dose of carbon monoxide can be measured in antimortem or postmortem blood by determining the carboxyhemoglobin levels. A second type of community study therefore has been to correlate carboxyhemoglobin levels either in living individuals or among deaths usually due to cardiovascular disease with clinical or postmortem changes. A major problem in these studies is the lag between exposure and measurement and the need to obtain a cigarette smoking history, as well as occupational exposure. Studies of sudden death especially deaths which occur within moments to individuals free of prior cardiovascular disease present a possible sentinel of carbon monoxide exposure relationship to heart attacks. About 20% of all heart attacks fall into this category and represent an interesting population for study. Furthermore, it is now possible by combining carboxyhemoglobin measurements with thiocyanate to adjust to some degree for reported cigarette smoking status.

Previous studies in Baltimore (*15*) and Los Angeles (*17*) have analyzed postmortem blood carboxyhemoglobin levels, among sudden deaths due to arteriosclerotic heart disease and other causes. The Baltimore study did not identify any evidence of high levels of carboxyhemoglobin among arteriosclerotic heart disease sudden death that were previously non-cigarette smokers. The Los Angeles study was also inconclusive. The number of sudden deaths due to arteriosclerotic heart disease among nonsmokers was relatively small and further expansion of these studies especially with more sensitive methods of measuring carboxyhemoglobin and thiocyanate levels as a marker of cigarette smoking may enhance their utility in the future.

The occupational studies have either attempted to measure the risk of death among men exposed to carbon monoxide or the prevalence of symptoms or specific electrocardiographic changes among men occupationally exposed to carbon monoxide. The extensive mortality follow-up studies of steelworkers in the United States by

Redmond et al. (*18*) and the British blast furnace studies (*10*) have both failed to identify any increased risk of cardiovascular disease. A study of Finnish foundry workers also did not find any excess cardiovascular mortality (*19*). Redmond (*20*) tried to determine the relationship between hot environments and cardiovascular mortality within the steel industry. She did not measure carbon monoxide levels in these areas but presumably they were correlated to some degree with the hot environment. She did not find any evidence of an increase risk of cardiovascular mortality associated with a hot environment.

Several morbidity studies of cardiovascular diseases have been done. The British foundry workers study did not identify any excess cardiovascular morbidity among the steelworkers as compared to the general population in spite of obvious increased carbon monoxide exposures and high levels of carboxyhemoglobin present in the workers (*10*). The Finnish foundry study compared workers in high carbon monoxide exposures and low in relationship to cardiovascular morbidity (*19*). Of heavy carbon monoxide-exposed nonsmoking furnace men and casters, 36% had carboxyhemoglobin levels greater than 6%, as did 71% of the occupationally exposed cigarette smokers. There were no differences between the exposed and nonexposed in electrocardiographic changes, but exposed smokers or nonsmokers had a higher prevalance of angina pectoris based on the Rose Questionnaire than the nonexposed. The exposed cigarette smokers had the highest prevalence of angina pectoris.

The occupational studies have serious limitations as currently designed because the highest risk workers will often move out of the exposed area because of symptomatology or health problems related to doing the type of work that is necessary. The mortality studies include both sudden and nonsudden deaths and do not separate those men who have their heart attack on the job from those that have a heart attack off the job. Since the carbon monoxide exposures may be acute precipitating events for heart attack, it would probably be more advisable to study the distributions of heart attacks on the job in relationship to carbon monoxide exposure, and perhaps carboxyhemoglobin levels. It also would be necessary to separate first heart attack deaths from individuals who die subsequent to a heart attack years after they have left the job. Also the attributable risks due to carbon monoxide exposure may be extremely low in comparison to smoking, blood pressure, cholesterol, etc., and difficult to identify in large population samples. Future occupational studies will have to have a more efficient design if the potential carbon monoxide exposures and cardiovascular morbidity and mortality are to be evaluated.

The clinical, experimental studies have provided the richest source of information about the relationship between low dose carbon monoxide exposure and heart disease (Table 7). Many of these studies have been previously reviewed.

In the classical study, high risk individuals, usually with angina pectoris, are exposed to a dose of carbon monoxide that will raise the carboxyhemoglobin level to some predetermined level, such as 2% to 4% carboxyhemoglobin. The men are then exercise tested on either a bicycle or treadmill and their responses evaluated. The end point was usually time of symptomatology, product of systolic blood pressure and pulse at the time of symptoms and ECG changes especially ST-T waves. Most of the recent studies have been double blinded.

Aronow has studied men with angina pectoris (*2*), intermittent claudication (*21*), and chronic obstructive pulmonary disease (*22*) (Table 8). Adverse health effects have been noted with carboxyhemoglobin levels as low as 2%. This method is clearly very sensitive to the study of low dose carboxyhemoglobin levels. However, the approach is different from the type of exposure in the general population since the carboxyhemoglobin levels are established by breathing relatively high concentrations of carbon monoxide (i.e., 50 ppm for 1 hr) in order to reach the desired carboxyhemoglobin level in the blood rather than relatively low dose exposure to carbon monoxide for longer periods of time. The importance of this difference in exposure, however, is undetermined. Aronow has also attempted to use this model to study behavioral effects. The studies have been inconclusive (*23*).

Davies and Smith (*24*) recently completed an important study of low dose carbon monoxide exposure and electrocardiographic changes among healthy nonsmoking young men (Table 9). Six groups of healthy, nonsmoking young men lived in a closed environmental exposure chamber for 18 days (Table 9). During the middle 8 days they were exposed to 50, 15 or 0 (control) ppm of carbon monoxide. P-wave changes on the electrocardiogram were seen in 6 of 15 subjects at 50 ppm and 3 of 15 at 15 ppm, but in none of the controls. It was possible that the P-wave changes may represent a toxic effect of carbon monoxide on atrial pacing and conduction tissue.

These studies more closely respond to the true environmental studies. The effects in normal

Table 7. Recent clinical and animal experimental studies of the relationship between carbon monoxide and disease.

Study	Methods	Results	Reference
4% Carboxyhemoglobin on human performance in cardiac patients	Double-blinded crossover study, 20 men with angina pectoris, COHb to 3.9%	Significant impairment of visualization test after breathing CO	(*23*)
Effect of nonnicotine cigarettes and CO on angina	Double-blinded crossover, 12 men, COHb to 5.35%	Decreased exercise time to angina > ST-segment depression: decreased systolic BP × heart rate at angina worse for smokers	(*23*)
Aggravation of angina pectoris by 2% carboxyhemoglobin	Double-blinded, randomized, crossover study, 15 men 50 ppm CO, 1 hr raise COHb to 2.02%	Decrease exercise to angina; decrease in systolic BP × heart rate at time of angina	(*23*)
Effect of passive smoking on angina pectoris	Ten patients with angina exposed to 15 cigarette smokers within 2 hr in a well-ventilated room or unventilated room; well-ventilated room COHb to 1.77, unventilated to 2.28	Passive smoking caused angina to develop sooner; worse in unventilated room; increased systolic BP and heart rate at angina	(*8*)
Electrocardiographic changes in healthy men during continuous low-level carbon monoxide exposure	Six groups of healthy young men living in a closed-environment exposure chamber for 18 days; exposed to 50, 15 or 0 ppm CO	P-wave changes on ECG at both 50 and 15 ppm of CO	(*24*)
Angina pectoris, ECG findings and BP of foundry workers in relation to CO exposure	Prevalence study in foundry in relation to CO exposure	Higher prevalence of possible angina history but not ECG changes with greater CO exposure	(*19*)

Table 8. Mean carboxyhemoglobin levels in three population studies (nonsmokers).

Study	Mean	% >1.5	Reference
St. Louis (1974)			(*31*)
Industrial workers	1.38 ± 0.040		
Nonindustrial workers	0.75 ± 0.013		
Nationwide survey (1974) (blood donors)			(*12*)
Los Angeles	1.8	76	
Chicago	1.7	74	
Vermont	1.2	18	
Denver	2.0	76	
HANES II			(*11*)
Never smokers	0.87 ± 0.74	08	
Center city[a]	1.10 ± 0.59	16	
Not center city[a]	0.97 ± 0.78	12	
Rural[a]	0.76 ± 0.63	05	

[a]White adults only.

young individuals are surprising and a possible cause for concern. They clearly need to be replicated, as well as similar studies, using high risk individuals.

The recent animal experimental studies have either attempted to determine the role of carbon monoxide in promoting the development of atherosclerosis or on lipoprotein metabolism or the effects of carbon monoxide on ventricular fibrillation threshold. The atherogenesis studies are conflicting but carbon monoxide exposure may increase atherogenesis in the presence of a high fat or cholesterol diet in a susceptible individual (*25*).

Table 9. Electrocardiographic changes in healthy men during continuous low level carbon monoxide exposure.[a]

CO run	Mean CO level during exposure period, ppm	No. of subjects	No. showing ECG changes during exposure
I (pilot)	75	10	7
II	50	9	4
III	0 (control)	8	0
IV	15	9	3
V	0 (control)	6	0
VI	50	6	2
VII	15	7	1

[a]Data of Davies and Smith (*24*).

Several studies have shown that relatively high levels of carbon monoxide usually around 100 ppm decrease the ventricular fibrillation threshold in both the dog and primate (Table 10) (*26*). This essentially means that a lower electrical shock for a shorter period of time will result in ventricular fibrillation in the presence of carbon monoxide. Studies have also shown that the threshold is lowered both in normal animals and those with a previously induced myocardial infarction (*27*). These studies are attempting to replicate the experience of sudden death in man. The availability of large numbers of individuals monitored by mobile coronary care units outside of the hospital may make it possible to do more extensive studies of the relationship between ventricular fibrillation, sudden death and environmental carbon monoxide exposures.

The carbon monoxide standard has not been based on possible health effects to the fetus and newborn. Previous animal experimental and human pathology studies have described an apparent effect of carbon monoxide on fetal growth and placental pathology (*1*). Epidemiological studies have determined that women who smoke during pregnancy have babies with low birth weights, increased perinatal mortality and certain complications of pregnancy and delivery (*28*). The specific effects of carbon monoxide independent of other products of cigarette smoke have not been determined. An increasing number of women are employed during their pregnancy. The possibility that women, both cigarette smokers and nonsmokers, may be exposed to an increased risk of low birth weight babies, higher perinatal mortality and complications due to exposure to carbon monoxide even at low dose must be considered. Studies to evaluate this potential risk, however, will be very difficult to design.

Discussion

There is little evidence to suggest that the current carbon monoxide standard is too high. The more critical question now relates to whether the clinical-experimental studies can be related to any substantial health risk in the population. The key determinants of whether current ambient carbon monoxide levels are hazardous relate to the size of the population at risk, the exposure dose and the excess risk per increased dose. There is no way at the present time of determining the exact increased risk associated with any specific level of carboxyhemoglobin. We can only accept the fact that 2% carboxyhemoglobin is associated with an apparent increased

Table 10. Recent animal experimental studies of the relationship between carbon monoxide and disease.

Study	Methods and results	Reference
Effects of carbon monoxide inhalation on ventricular fibrillation in monkeys	Exposure to 100 ppm CO 9.3% increase in COHb Ventricular fibrillation threshold increases in both infarcted and normal monkeys	(*26*)
Carbon monoxide and ventricular fibrillation threshold in normal dogs	100 ppm CO for 2 hr Increase COHb 6.48% Decrease ventricular fibrillation threshold	(*27*)

symptomatology among patients with angina pectoris. Whether this can be translated into an increased risk of heart attack and sudden death has not been adequately determined. Only one study has determined that relatively low doses of carbon monoxide are associated with possible changes in the electrocardiogram in normal individuals which might relate to cardiovascular disease (*24*). The results reported in that study, that is, the P-wave changes, must be further evaluated prior to their use as part of the carbon monoxide standard setting activities. The most important population at risk are probably individuals with clinical heart disease, chronic obstructive pulmonary disease and intermittent claudication.

Data describing the prevalence of heart disease in the community is surprisingly difficult to obtain. The National Health Interview Survey in 1973 provided information about the prevalence of heart disease 13.6/1000 (*29*), and chronic bronchitis, 32.7/1000 (*30*). These are probably underestimates, since they are based on interview only and not on physical examination. Still, however, a substantial percentage of the United States population has either a known history of heart disease or chronic obstructive pulmonary disease and would be considered at high risk for low dose carbon monoxide effect.

The percentage of the population overall exposed to carbon monoxide levels which result in carboxyhemoglobin levels above 1.5 to 2% has fallen if one compares the data from previous studies and that of the Hanes II report, as provided by Radford (Table 9). As previously mentioned, the reasons for the differences in the levels reported by these studies may not only be due to decreases in air pollution but also to sampling and methods of measuring carboxyhemoglobin. However, even using the data from Radford's study, a substantial portion of the U.S. adult

population, probably over 10 million, is exposed to potentially deleterious levels of carbon monoxide. Presuming that 75% of patients with coronary heart disease are nonsmokers and that the prevalence of coronary heart disease among adults is about 20/1000 would result in approximately 170,000 persons with heart disease who are nonsmokers and might have major effects from low dose environmental carbon monoxide exposures. The cigarette smokers obviously would also be exposed since the ambient carbon monoxide level would enhance the cigarette smoking effects. Furthermore, if we presume that 20–30% of all patients with heart disease have major coronary artery disease symptomatology that will increase their risk of heart attack and sudden death, then there may be 35,000–50,000 people at high risk. If we were to further presume that their risk of death was about 5% per year and that carbon monoxide exposure doubled the risk, then perhaps 1250 excess deaths related to low dose environmental carbon monoxide exposure in this population might be noted each year in the United States. This analysis is obviously crude and excludes many individuals who have severe coronary artery disease, were asymptomatic and may die suddenly when exposed to carbon monoxide, patients with chronic obstructive pulmonary disease who also apparently are at increased risk or the large number of pregnant women each year who may have increased perinatal mortality and low birth weight babies.

There is clearly a need to determine whether the increased risks noted by these clinical, epidemiological and animal experimental studies can be translated into true risks in the community. These studies should primarily be aimed at high risk populations such as occupationally exposed groups to high levels of carbon monoxide, groups at high risks due to disease such as patients with heart disease and chronic obstructive pulmonary disease and pregnant women.

The monitoring of carbon monoxide in the community should depend primarily on the measurement of carboxyhemoglobin levels and not on ambient carbon monoxide monitoring in the community. The clinical laboratory studies previously done by Aronow et al. should be replicated in other laboratories with longer exposures at lower doses of carbon monoxide and with more subjects per experiment. The interesting long-term chamber studies must be replicated (*24*). If the results of those studies can be validated by other investigators, then the importance of low dose carbon monoxide exposures may be much greater than anticipated.

Finally, it should be recognized that the major source of carbon monoxide in the population is cigarette smoking. The effects of low-dose ambient carbon monoxide exposures from all other sources on the health of the population is minimal compared to the effects of cigarette smoking. Thus, reduction of cigarette smoking in the population should certainly remain the highest public health priority.

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